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Medical Information

Serum Thyroid Hormones in Patients on Replacement or Suppressive Doses of L-Thyroxine

SIDNEY ROSENBLATT, MD
JEROME M. HERSHMAN, MD
Los Angeles

ABBREVIATIONS USED IN TEXT

T_3 = triiodothyronine
T_4 = L-thyroxine
TSH = thyroid-stimulating hormone

CHANGES IN THE normal circulating levels of thyroid hormones occur in patients taking replacement or suppressive doses of L-thyroxine (T_4). Most of the circulating pool of triiodothyronine (T_3) is derived from peripheral monodeiodination of thyroxine.[1-3] Adequate treatment with L-thyroxine usually produces serum T_4 levels similar to or slightly higher than control values, T_3 levels are often slightly lower than controls, and the T_4/T_3 ratio would be expected to be higher than control values. We measured serum concentrations of T_4, T_3 and thyroid-stimulating hormone (TSH) in patients with a variety of thyroid disorders to assess the significance of changes in circulating thyroid hormone levels in patients taking L-thyroxine.

Methods

A retrospective analysis was made of 132 patients receiving adequate suppressive or replacement doses of L-thyroxine. A total of 71 patients were in the hypothyroid group, and 61 were in the euthyroid group being treated for nodular or diffuse goiter. Patients with autonomously functioning nodular goiters were not included. The dose range was 0.1 to 0.3 mg of L-thyroxine, and adequate treatment was assessed by normal concentrations of serum thyrotropin (less than 5 μU/per ml) in all patients without pituitary disease. The patients with pituitary disease all had normal levels of serum T_3 and T_4. Serum T_3, T_4 and TSH were measured by radioimmunoassays.[4] All patients were receiving therapy for at least three months. The patients were otherwise

From the Endocrinology Section, VA Wadsworth Medical Center, Los Angeles, and the Department of Medicine, University of California, Los Angeles, School of Medicine.

Supported by the Medical Research Service of the Veterans Administration.

Reprint requests to Sidney Rosenblatt, MD, Endocrinology Section, Wadsworth VA Hospital, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073.

healthy which excluded non-thyroidal alterations in serum thyroid hormones.

A total of 161 patients without thyroid disease served as normal controls. The age patterns in the controls and treated groups were similar. Statistical significance was determined by Student's t-test.

Results

Table 1 shows the serum T_3, T_4, T_4/T_3 ratio and TSH in the control group and the groups treated with various doses of L-thyroxine. Serum T_4 concentrations and the T_4/T_3 ratio were higher in all the treatment groups irrespective of dose ($p<0.05$). Serum T_3 concentrations were elevated significantly only in the euthyroid treated patients. Serum TSH was undetectable (less than 0.3 μU/per ml) in 58 percent of all patients treated for primary hypothyroidism and 72 percent of all patients in the euthyroid treated group.

When patients in both treatment groups were selected because their serum T_4 was in the lower half of the normal range (5 to 8.5 μg per dl), the T_4/T_3 ratio was 51.4 in the hypothyroid and 48.0 in the euthyroid treated groups. These values were similar to the ratio in untreated controls. The mean T_3 level was 143±29 ng per dl in the hypothyroid treated groups and 150±26 ng per dl in the euthyroid treated groups, which are similar to T_3 concentrations in controls.

Discussion

The data show that T_4 concentrations and the T_4/T_3 ratio in patients receiving replacement or suppressive doses of L-thyroxine are increased. T_3 levels are normal or increased. Higher levels of thyroid hormones were observed in patients treated for goiter suppression because the therapeutic goal was suppression of endogenous TSH secretion.

In patients taking the usually prescribed doses of L-thyroxine, the T_4/T_3 ratio may be altered for two reasons. Firstly, the serum T_4 level is elevated, suggesting that these doses of L-thyroxine are too high. The mean T_4 level in the hypothyroid group was 2.6 μg per dl higher than the mean control value of 7.6 μg per dl, and the mean T_4 value in the euthyroid group was 3.7 μg per dl higher than the controls. To further elucidate this point, we selected those patients receiving therapy who had T_4 levels between 5 and 8.5 μg per dl. Their T_3 levels and T_4/T_3 ratios were unchanged from those of controls. Therefore, the alterations in thyroid hormone relationships is primarily affected by the serum T_4 level. Second, the circulating levels of T_3 in patients taking L-thyroxine is derived primarily from peripheral monodeiodination.[1-3] The reduced thyroidal contribution of T_3, secondary to suppression or loss of thyroid secretion, probably also plays a role.

TABLE 1.—*Serum Thyroid Hormone Concentrations (Mean ± S.D.)*

GROUP	T_4 dose mg	No.	T_4 μg/dl	T_3 ng/dl	T_4/T_3	TSH μU/ml	Undetectable TSH (Percent)
Normal	0	161	7.6 ±1.6	153.7 ± 32.7	50.8 ± 13.1	1.8 ± 1.6	4.3
Hypothyroid	0.1-0.15	34	9.2* ±2.4	168.8 ± 64.4	59.4* ± 23.2	1.3* ± 1.6	44‡
Hypothyroid	0.2	27	11.3† ±4.6	173.6 ± 44.0	64.3* ± 17.1	1.1* ± 2.3	66‡
Hypothyroid	0.25-0.30	10	10.6† ±3.4	175.1 ± 22.2	59.3* ± 12.3	0.3† ± 0.8	89‡
Euthyroid	0.1-0.15	11	10.0† ±3.2	173.7* ± 64.8	59.7* ± 13.2	0.5† ± 0.8	63
Euthyroid	0.20	34	11.1† ±3.3	181.5* ± 45.5	63.2* ± 15.0	0.4† ± 0.7	71
Euthyroid	0.25-0.30	16	12.7† ±3.0	186.3* ± 49.0	70.1* ± 14.5	0.1† ± 0.2	81
All hypothyroid		71	10.2† ±3.5	171.5 ± 52.4	61.2* ± 19.7	1.1* ± 2.1	58
All euthyroid		61	11.3† ±3.3	181.4* ± 49.5	64.4* ± 14.8	0.3† ± 0.6	72

T_3 = triiodothyronine T_4 = L-thyroxine TSH = thyroid-stimulating hormone

*P<0.05 compared with normal untreated subjects
†P<0.005
‡Patients with primary hypothyroidism only

By using a sensitive radioimmunoassay for TSH, we showed that most patients taking L-thyroxine had undetectable levels. Nearly all normal and untreated euthyroid goitrous patients have detectable circulating levels of TSH with this assay. We agree with Stock and co-workers[5] that the current textbook recommendations for replacement therapy with L-thyroxine are too high. We recommend 0.1 to 0.2 mg of L-thyroxine for replacement therapy. Suppression therapy with this dose range will effectively reduce TSH to undetectable levels in most patients; however, the dose must be individually tailored for each patient.

Summary

Serum thyroid hormones were measured in patients taking L-thyroxine for replacement or suppressive therapy. Their serum T_4 levels and T_4/T_3 ratios were greater than controls and their serum T_3 levels were normal or slightly increased. This finding was more evident in the euthyroid goitrous group because higher doses of thyroxine were used to suppress TSH secretion. Serum TSH levels were suppressed to undetectable levels in most patients. Replacement therapy for hypothyroidism can be achieved with 0.1 to 0.2 mg of L-thyroxine which will suppress serum TSH to undetectable levels in most patients.

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Herpes Zoster Keratouveitis

YOU SHOULD ALL REMEMBER that those who have herpes zoster keratouveitis in the older age group may very well have an underlying malignancy, and that should be looked for.

—PETER R. LAIBSON, MD, *Philadelphia*

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